clinically to isolate specific blood cell types or pathogens from batches of pooled blood (e.g., stem cells for bone marrow reconstitution procedures in cancer patients.). In the conventional method, a large group of bead-bound cells are statistically pulled out of the remaining blood contents all at once using a tube filled with steel wool surrounded by a stationary magnet. This method is labor intensive and lacks accuracy, especially when a certain type of cells needs to be "completely" cleared.

[0197] Additionally, the cell sorting methods and apparatus discussed above facilitate parallel fluid processing with multiplexed microfluidic channels and CMOS circuits. CMOS electronics also makes possible automation in cell sorting. In comparison with fluorescence-activated cell sorters (FACS), a system according to the concepts discussed herein may be implemented in a much smaller and less expensive manner. Moreover, a cell sorting system according to the present disclosure requires minimal preparation of the cells for sorting (e.g., no transfection of fluorescent proteins). Additionally, in another aspect, it is arguably easier to maintain physiological homeostasis with a microfluidic system than any large volume device.

[0198] According to various aspects of the embodiment illustrated in **FIG. 40**, a number of practical considerations may influence the cell sorting process. For example, some variables that may affect cell sorting include, but are not necessarily limited to: 1) efficiency of ligand-receptor binding on targeted cells; 2) incidence of nonspecific binding of the beads to non-targeted cells; 3) the number of cell types in the solution; 4) the density, or cells per liter, of the suspension; and 5) the efficiency with which cells have been dissoluted from a harvested tissue or organ. The first and second variable may be addressed by selecting ligands that are specific to cell surface receptors uniquely expressed by the targeted cell type.

[0199] For example, by targeting endothelial cells in one exemplary implementation, PECAM is an ideal choice of cell surface molecules because of its unique expression in endothelial cells and because of its role in cell mobility and cellular adhesion; as a result, the likelihood of detachment of the bound magnetic bead during transit is reduced. In another implementation, endothelial cells may be sorted from a cell suspension also containing NIH 3T3 fibroblasts which do not express PECAM. The throughput rates and density of the cell suspensions may be calibrated for optimal sorting performance.

[0200] Also, in other implementations, an iterative process may be employed, wherein experimental parameters optimized in a first sorting process serve as the initial conditions for one or more subsequent sorting processes, such that cells may be sorted from suspensions containing multiple cell types. For example, in one process involving the neonatal heart, endothelial cells may be separated from cardiac myocytes, fibroblasts, immune cells that have extravasated prior to harvest, and neural tissue. The 'noisy' environment created by this mixed cell population in some cases determines the boundaries of cell sorting performance. In one aspect, diluting the cell suspension may increase the time required for sorting, but may increase sort accuracy. In another aspect, to assure sufficient dissolution, a suspension may be passed through a filter that selectively filters large cellular ensembles that have evaded dissolution by trypsin and collagenase.

[0201] VII. Tissue Assembly

[0202] In yet another embodiment according to the present disclosure, micro-scale assembly of engineered tissues may be realized using the various methods and apparatus discussed herein. For example, in one implementation, assembly of micro-scale, engineered cardiac tissues from heterotypic cell populations is accomplished utilizing a CMOS/microfluidic hybrid system **100** as discussed herein.

[0203] A complex signaling dialogue between multiple cell types in a tightly constrained space that is reorganizing with each developmental step mediates tissue morphogenesis. In the mature tissue, the spatial and demographic control of these cell populations is strenuously maintained but its loss marks the onset of the disease process in a recognizable fashion. What is unknown is how the subtle interactions of seemly controlled cell populations can potentiate pathogenic events. An excellent example of this is the cell-cell interactions between capillaries and cardiac muscle fibers in the heart, which alters action potential propagation, contributing to arrhythmogenesis. This is an important problem because there is currently no clinically reliable means of treating cardiac arrhythmias medicinally. Furthermore, antiarrhythmic drug pipelines at pharmaceutical and biotechnology companies are barren, in part due to a lack of experimental assays that support the identification of new drug targets. Thus, the ability to engineer micro-scale cardiac tissues of heterogeneous cell populations offers reliable, effective assays of cardiac arrhythmia for the discovery of new drug targets and the elucidation of answers to fundamental questions in cardiac electrophysiology.

[0204] More generally, heterotypic signaling between different cell populations defines the tissue micro-environmental changes in tumors, the heart, and liver. Therefore, micro-scale tissue assembly is important to study communication networks amongst different cell types, drug efficacy, and for fundamental physiological study in a standardized, repeatable manner. However, precise engineering of model tissues on micro-scale has proven difficult.

[0205] Several techniques for heterotypic cell culture with population control exist. Transwell plates have traditionally been used to study paracine signaling between two distinct cell populations. New techniques for mimicking the tissue microenvironment in vitro have relied on photolithographic techniques. One known strategy is based on using patterned photoresists or masks to allow cell attachment to select regions of a surface. Subsequent removal of the resist or mask reveals areas amenable to a second cell type's adhesion. A second strategy exploits dielectrophoresis to pattern and separate cervical carcinoma cells from red and white blood cells on a microelectrode array. Other strategies include microfluidic channels to direct cell suspensions to different locations on a surface, an electroactive mask that allows seeding of a second cell type to regions of a surface that were electrically activated to permit attachment, and gravity-enforced tissue assembly. These techniques have proven to be labor intensive, lacking precise population control, and slow. The technique based on dielectrophoresis is interesting, because it represents a strategy for cell sorting and micro-scale tissue reconstruction; however, it lacks the accurate cell population control required to do quantitative studies, the spatial control afforded by micropatterning technologies, and is reliant upon the cells having distinct polar-